REMARKS/ARGUMENTS

In the Office Action, the Examiner rejected claims 1-12 and 16-27 based on the new ground that the amendments made to these claims introduced new matter. The Examiner further maintained the lack of enablement rejection raised previously under 35 U.S.C. 112, first paragraph. Each rejection is considered separately below.

A declaration by Dr. Marcin Filutowicz is attached to provide evidence that the claims are enabled. Dr. Filutowicz is a highly accomplished and well-known and respected scientist in the field of Microbiology. He was recently invited by the American Society of Microbiology (ASM) to write a chapter on plasmid replication for the book "Plasmid Biology" that ASM will publish. Dr. Filutowicz was also recently invited by Nature Structural Biology to write a commentary on plasmid replication for the journal.

A petition for one month extension of time accompanies this response so that the response will be deemed to have been timely filed. If any other extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to the Deposit Account No. 17-0055. No other fee is believed to be due in connection with this response. However, if any fee is due in this or any subsequent response, please charge the fee to the same Deposit Account No. 17-0055.

I. New matter rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 1-12 and 16-27 reasoning that the applicant had not set forth any support in the specification for the term "recombinant bacterium" recited in the amended claims. The applicant respectfully directs the Examiner attention to page 14, line 21 of the application where the term "recombinant bacteria" is used to refer to the bacteria described earlier in the specification, which are the same as the bacteria in the pending

claims. In addition, Example 2 specifically disclosed a recombinant bacterium as claimed. Therefore, the amended claims are supported by the specification.

II. Lack of enablement rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 1-12 and 16-27 alleging that the specification does not provide substantive evidence that the claimed antibacterial agent can maintain stability or that the antibacterial agent is capable of treating bacterial infection (see page 4 of the Office Action, lines 18-21). In the Examiner's opinion, a skilled artisan would not be able to reasonably predict whether the claimed invention could survive *in vivo* use or would be able to treat bacterial infection (see page 4 of the Office Action, lines 21-26). The Examiner is especially concerned with the lack of 37 C.F.R. 1.132 declaration or other evidence in the record to establish the amount of experimentation necessary to practice the present invention (see page 5 of the Office Action lines 41-43). The Examiner further determined that the specification did not provide sufficient guidance and working examples so that undue experimentation is needed to use the present invention to treat bacterial infection (see page 5 line 43 to page 6 line 10 of the Office Action). The applicant respectfully disagree with the Examiner's positions.

(1) For composition claims 1-12 and 16-27, the applicant only needs to enable one use: enablement for *in vivo* pharmaceutical use is not necessary if another use is enabled.

For a composition claim, one needs to teach how to make and use the composition to satisfy the enablement requirement. However, the enablement requirement does not ask for all possible uses to be enabled. As long as the inventors teach and enable one use, the enablement requirement is satisfied. For example, if an inventor discovered a new chemical that can kill bacteria as well as tumor cells, as long as the inventor teaches people how to use the chemical as a disinfectant (killing bacteria), a composition claim for the chemical should

satisfy the enablement requirement even though the inventor has not taught people how to use the chemical to treat cancer, in which case a method claim for treating cancer may have an enablement problem.

In the present invention, the *in vivo* pharmaceutical use of the claimed compositions is only one of the uses described in the specification. The specification disclosed that the compositions can also be used on meat and other food, including animal feed, to eliminate pathogenic bacteria (see page 16, lines 17-19 of the specification). If the latter use is enabled, the claims should be considered enabled regardless whether the *in vivo* pharmaceutical use is enabled.

(2) Use of the claimed recombinant bacteria for eliminating pathogenic bacteria in animal feed is enabled.

The pending claims are directed at recombinant bacteria that contain a transmissible plasmid having an origin of replication, an origin of conjugative transfer, a screenable marker and a mechanism for killing recipient cells. The killing mechanism can be either run-away replication or a killer gene. The recombinant bacteria either contain repressors to suppress run-away replication or are modified to be unaffected by the product of the killer gene. The recombinant bacteria further contain transfer genes for the conjugative transfer of the plasmid.

The specification described all of the above essential features of the recombinant bacteria as claimed and provided examples for what can be used to build these bacteria. Examples 1 and 2 specifically showed that the recombinant bacteria can be made. Given the state of the microbiology and molecular biology art at the time the application was filed and the ordinary skill level in the art, a skilled artisan can readily make the recombinant bacteria as claimed.

A skilled artisan can also readily use the recombinant bacteria to eliminate pathogenic bacteria in animal feed as provided in the specification. No undue experimentation is necessary according to Dr. Filutowicz's declaration. Experimental data provided in the declaration showed that bacteria containing either of the two plasmids constructed according to the claims, E. coli S17 containing plasmid pFL415 that is designed to kill recipient bacteria through run-away replication (corresponds to a recombinant bacterium in claims 1-12) and E. coli S17 containing a plasmid that is designed to kill recipient bacteria through the expression of the bacteriocin gene colE3 (corresponds to a recombinant bacterium in claims 16-27), were able to kill bacteria of multiple species and strains as predicted in the application. Dr. Filutowicz confirmed in the declaration that the construction of the plasmids and the use of the recombinant bacteria to kill target bacteria were accomplished by following the teaching of the application using mature technologies in the art. No undue experimentation was involved. In fact, once the recombinant bacteria were made, they were simply mixed with the target bacteria on a filter at either 30°C or 37°C and the plasmids were able to transfer from the donor cells to recipient cells to kill the recipient cells. This or similar conditions can be easily duplicated in animal feed so that the pathogenic bacteria therein can be killed (see Dr. Filutowicz's declaration attached).

In making the rejections, the Examiner was concerned about the stability of the plasmid in donor cells, during conjugative transfer and in recipient cells. The Examiner cited four references (Ambrozic, et al., Klimke et al., Roberts et al. and Rahal et al.) to show that various factors may affect plasmid stability. Without any experimental evidence, the Examiner was not prepared to accept that these factors will not interfere with the practice of the present invention. The applicant herein provides experimental data through Dr. Filutowicz's declaration to show that donor cells containing the plasmids were successfully made and mixing the donor cells with the recipient cells led to the killing of the recipient

cells. The experimental data further showed that the recombinant bacteria were able to kill target bacteria from multiple species and strains. Therefore, plasmid stability did not present a problem to the successful use of the recombinant bacteria. Furthermore, as Dr. Filutowicz provided in the declaration, even if plasmid stability presents a problem for a particular plasmid and bacterial strain in a particular application, a skilled artisan can readily solve the problem by using a plasmid and a donor bacterium derived from the same strain as the target bacteria. In this case, since the plasmid is derived from a natural plasmid of the target bacteria and the donor bacteria are of the same strain as the target bacteria, the plasmid should be very stable in both the donor bacteria and the target bacteria. The conjugative transfer of the plasmid will be between two bacteria of the same strain, from which the plasmid being transferred is derived, the plasmid should also be very stable during the conjugative transfer process. Since only mature technologies are involved to accomplished the above, a skilled artisan can readily do it without undue experimentation.

In conclusion, as demonstrated by Dr. Marcin Filutowicz's declaration, a skilled artisan can readily make the recombinant bacteria as claimed and use them to kill pathogenic bacteria in animal feed. In view of the declaration attached and the arguments provided above, reconsideration of the rejections is respectfully requested.

Respectfully submitted,

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